Invasive *Vibrio cholerae* Infection Following Burn Injury

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***Vibrio cholerae* is a pathogen predominantly appreciated for its potential to produce life-threatening watery diarrhea, usually without invasive disease. However, nonepidemic forms, which are present worldwide, may have a severe invasive presentation, especially among those with liver disease or other immunocompromised states. We present a case of invasive infection (pulmonary, wound, and bacteremia) by nonepidemic *V. cholerae*, in a soldier that sustained burn injury in Iraq. Multiple factors, to include burn injury and water exposure, likely contributed to this presentation. A brief discussion of the pertinent literature is included. (J Burn Care Res 2008;29:551–554)**

A 24-year-old Caucasian male was transferred to the U.S. Army Institute of Surgical Research burn unit in October 2006, 48 hours after sustaining 55% total body surface area burn injury (40.5% full thickness), to include significant burns to the face and head. The burn injury occurred as the soldier was traveling in a tracked vehicle under attack in Iraq. At the time of injury, the patient was placed in a nearby canal to extinguish the flames on his body. After undergoing basic stabilization, to include intubation and fasciotomies to all extremities, he was evacuated to a U.S. military hospital in Europe for additional medical care.

At this military facility, the imaging revealed mesenteric stranding in the vicinity of the duodenum and right colon, but exploratory laparoscopy was unremarkable. The patient also underwent external fixation of the right ankle and common plantar artery bypass for extensive wounds to the right lower extremity. He was then transferred to the U.S. Army Institute of Surgical Research. On arrival, the patient required mechanical ventilatory and pressor support. Admission chest x-ray examination revealed no infiltrates. Labs were significant for normal renal and liver chemistries, normal white blood cell count, a mild normocytic anemia, and a platelet count of 49,000/μL. In the first 24 hours after arrival, the patient underwent escharectomy and skin grafting, right lower extremity below the knee amputation, and was noted to have bilateral orbital compartment syndrome requiring cantholysis. Given that both blood and urine cultures performed earlier in the patient's care were displaying the growth of Gram-negative rods, the patient was started on empiric imipenem and once daily amikacin.

The patient's clinical course deteriorated soon after surgery, and he developed progressive sepsis in the setting of ventilator-associated pneumonia, acute respiratory distress syndrome, as well as acute renal injury, requiring continuous renal replacement therapy, continued pressor support, and airway pressure release ventilation. Multiple admission blood cultures revealed growth of multidrug-resistant *Acinetobacter calcoaceticus baumanii* complex, *Vibrio cholerae,* and *Stenotrophomonas maltophilia*. The former two isolates were also isolated from respiratory cultures. *V. cholerae* was also isolated from excised burn wounds of the left thigh. Cultures of stool and urine did not reveal *V. cholerae,* nor did blood, stool, urine, and sputum cultures of the other two occupants in the tracked vehicle. The patient was treated with a 7-day course of ciprofloxacin for his *V. cholerae* infection, as well as courses of colistin and tigecycline for his other multidrug-resistant Gram-negative rods infections, eventually resolving his *V. cholerae* infection and be-

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ing discharged from the hospital after a 172-day course.

The *V. cholerae* isolates had a stellate morphology on blood agar and a smooth morphology on thiosulfate-citrate-bile-salts-sucrose agar (TCBS) culture. The organism was identified via Vitek (BioMerieux, Durham, NC) and confirmed with the API-20NE system (BioMerieux, Inc.). Susceptibility testing, via the E-test method, revealed susceptibility (per Clinical Laboratory Standards Institute, CLSI standards) to tetracycline (minimum inhibitory concentration (MIC) 0.75 μg/ml). Additional testing also revealed MICs of <0.016 μg/ml for cefotaxime, 0.003 μg/ml for ciprofloxacin, 96 μg/ml for colistin, 4 μg/ml for amikacin, and 1.5 μg/ml for imipenem (no CLSI cutoff available). The isolate was forwarded to both the Texas State Department of Health and the Centers for Disease Control, confirming that the isolate was a non-O-1, non-O-139 serotype *V. cholerae*.

DISCUSSION

V. cholerae is a motile Gram-negative rod, with a characteristic "comma" shape (hence Robert Koch's labeling as *Komma bazillen* and later *Vibrio comma*). *Vibrio* species are part of the normal bacterial flora in estuaries worldwide and aquatic environments of varying salinities. Unlike epidemic cholera, concentrations of nonepidemic *V. cholerae* (NEVC) strains in the environment are typically not associated with that of fecal coliforms.[1] In the United states, the majority of *Vibrio* infections are secondary to *Vibrio vulnificus, Vibrio parahaemolyticus,* and *Vibrio alginolyticus*—NEVC being a rare but not uncommon etiologic agent.[2,3]

There is scant data pertaining to the epidemiology of *V. cholerae* in Iraq, and what is available does not describe nonepidemic strains. Epidemic cholera outbreaks in Iraq are described as recently as 2007, and cholera is considered endemic throughout Iraq.[4,5] Given that free-living NEVC counts are usually several-fold higher than epidemic strains in any given body of water, it can be assumed that nonepidemic strains are located throughout Iraq, making canal water exposure a plausible source of infection in our case patient.

NEVC infection may present as asymptomatic colonization, otitis, gastroenteritis, soft-tissue infection, sepsis, or even cerebritis. In contrast, epidemic *V. cholerae* (O-1 or O-139) predominantly manifests as diarrheal disease with rare presentations as invasive infection. Infection with *Vibrio* organisms is typically associated with water, fish, and/or shellfish exposure. Although invasive infection with NEVC has been reported in otherwise healthy individuals, as with other invasive *Vibrio* species, those with immunocompromised states, particularly liver disease, are at high risk for severe infection. Reported case fatality rates for invasive NEVC infection range from 47 to 65%, a mortality comparable to that of *Vibrio vulnificus*.[6–8] Septicemia is not uncommonly associated with rapid clinical decline and death. Similar to advanced liver disease, burn victims experience a significant impairment in cell-mediated immunity, to include deficits in

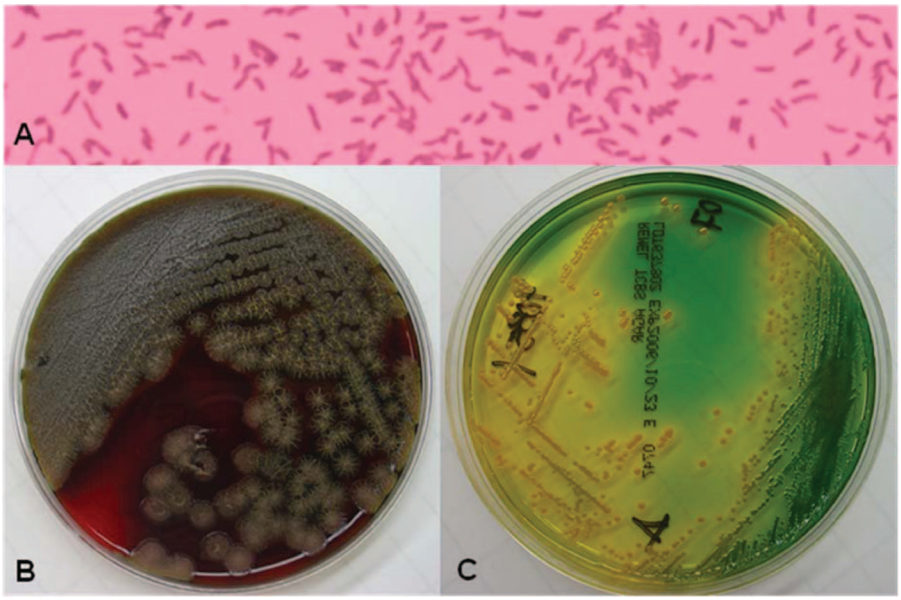

Figure 1. A. Gram stain of Gram-negative curved bacilli of *V. cholerae* from blood culture. B. Rough, stellate colony morphology of *V. cholerae* on blood agar. C. Smooth, yellow colonies of *V cholerae* on TCBS agar.

Table 1. Published cases of NEVC infection in association with burns and/or pneumonia

Reference Citation	Age (yr)	Sex	Predisposition	Associated Water Exposure	Sites of Isolation	Outcome
12	32	M	63% TBSA* burn	Well water used to extinguish flames	Blood	Survival with 81-d hospital course
13	25	F	50% TBSA burn	Immersion in river	Sputum	Resolution of NEVC pneumonia, but eventual death secondary to burn injuries
13	67	M	Alcoholism, alcoholic liver disease	Aspiration after falling into a drainage ditch	Sputum and blood	Survival after a 6-d hospital course
7	58	M	None	Near drowning in pond	Sputum	NEVC and *Vibrio vulnificus* isolated. Died 24 hr after admission of pneumonia/ARDS

**TBSA,* total body surface area burn.

reticuloendothelial system function, neutrophil chemotaxis, and T-cell function. Other shared immune defects include some degree of immunoglobulin deficit as well as depressed complement and opsonic activity.[9,10] These common immune deficits may place burned patients within the cohort at risk for NEVC infection. An interesting theme, among reports of invasive infection with NEVC, is large volume water exposure or the ingestion of shellfish (which may have >100 times the concentration of organisms compared with surrounding waters), suggesting that large inoculum exposure (as is likely in the presented case) is another significant risk for disease with this organism.[1,11]

NEVC and epidemic strains are virtually indistinguishable in culture and upon biochemical testing, usually requiring agglutination with polyvalent antiserum for identification. *V. cholerae* grows well on common blood agar, with decreased bacterial overgrowth on selective media, such as TCBS agar. As noted in our case (Figure 1), it is possible for both epidemic and nonepidemic strains to have a "rugose" phenotype on nonselective media, and usually a smooth phenotype on TCBS.[11] One notable difference between epidemic and NEVC is the production of a polysaccharide capsule in >90% of nonepidemic strains. Akin to other invasive *Vibrio* species, such as *Vibrio vulnificus*, heavily encapsulated NEVC strains are associated with increased virulence and are more likely to present as invasive disease.[1,11] NEVC strains are generally felt to have a low rate of antibiotic resistance compared with other enterobacteriaceae, with agents similar to those used for treatment of *Vibrio vulnificus* generally considered effective (minocycline and cefotaxime, or fluoroquinolone). This stated, the CLSI only provides susceptibility breakpoints for ampicillin, tetracycline, trimethoprim-sulfamethoxazole, sulfonamides, and chloramphenicol.

NEVC pneumonia among burned patients is a rare event. This patient appears to be the second published case of NEVC pulmonary infection in a burned patient (the third published case of burn associated NEVC infection, and the fourth case of pulmonary infection associated with this bacterium). A review of the available literature is presented in Table 1.

CONCLUSION

Infection with invasive *Vibrio* species bacteria (e.g. *Vibrio vulnificus, Vibrio alginolyticus, Vibrio parahaemolyticus*, NVEC, etc.) should be considered in those patients with a compatible clinical syndrome, high inoculum exposure (via a contaminated water or food source), and/or immunosuppression—to include burn victims. As is demonstrated by this case, clinicians should especially note that the isolation of *V. cholerae*, in the absence of gastrointestinal disease, may represent invasive NEVC infection.

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